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Case Report

Linezolid therapy for pediatric thoracic spondylodiscitis due to *Staphylococcus aureus* sepsis

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ABSTRACT

We report the case of an immunocompetent child with spondylodiscitis as a result of staphylococcal sepsis, which was successfully treated with linezolid. The patient was admitted with fever and circumferential swelling in the paradorsal region, which was evident only in the flexed back position. A chest X-ray showed a pleural effusion with pneumonitis and dorsal kyphosis. Following the yield of *Staphylococcus aureus* from blood cultures, the initial therapy of ceftriaxone and amikacin was changed to vancomycin. However, the dorsal swelling increased further and imaging investigations showed destruction of the vertebral bodies D8–D10 and surrounding tissue swelling. Vancomycin was changed to linezolid, and the patient began to improve; a full recovery was made. Our case suggests that even if spondylodiscitis is rare in the pediatric age-group, particularly as a complication of staphylococcal sepsis, early diagnosis and prompt and appropriate therapy are important to prevent severe complications.

1. Introduction

Pediatric spondylodiscitis is an uncommon entity, accounting for only 1–2% of all children with osteomyelitis, however the exact incidence is unclear.[1–4] The pathophysiology of child discitis and vertebral osteomyelitis remains poorly understood. It is less commonly seen in children younger than 3 years of age than in adolescents and adults, because the vertebral bodies of infants have a larger network of interosseous collateral arteries, which help clear bacteria.[5–8] At the same time, the relatively thin cortex and loosely applied periosteum are poor barriers to the spread of infection, hence young infants may be at risk of infection by less virulent organisms, which are often part of the normal flora in humans.[3,7,8] This is largely due to the poorly developed immune system of young infants, who are less able to build up a specific immune response. *Staphylococcus aureus* is the most common cause of osteomyelitis in all age groups on account of its peculiar tropism for bone tissue. The clinical efficacy of linezolid has previously been evaluated for staphylococcal osteoarticular infections in children.[9] Early diagnosis and appropriate therapy are crucial, both for survival and the prevention of long-term damage.[3,8,10,11] We report the case of a young infant with spondylodiscitis and sepsis by *S. aureus*.

2. Case report

A 45-day-old male infant, born by uncomplicated delivery at term, was admitted because of fever persisting for 24 h. There was no history of trauma, skin infection, central venous catheter, surgical or other invasive procedures. Two weeks before, the child had presented with pharyngitis treated with amoxicillin for 6 days.

On physical examination, the patient was pale with a hyperemic pharynx and a non-tender circumferential swelling of 3 cm in diameter in the paradorsal region, which was evident in the flexed back position. Laboratory investigations showed a leukocyte count of 31.39 $\times$ 10^9/l with 75.1% polymorphonuclear neutrophils, hemoglobin (Hb) level of 9.9 g/dl, platelet count of 567 $\times$ 10^9/l, C-reactive protein (CRP) of 27.83 mg/dl (normal value <0.5), erythrocyte sedimentation rate (ESR) of 127 mm/h, and increased levels of γ-glutamyltransferase (γ-GT <0.84 IU/l) and fibrinogen (675 mg/dl). Immunological investigations revealed increased levels of immunoglobulins (IgG 2169, IgM 149, IgA 323 mg/dl) and normal T-cell subsets. At admission, cultures of cerebrospinal fluid, urine and blood were negative. Radiographic examinations showed a pleural effusion with pneumonitis and dorsal kyphosis. Antibiotic treatment with amikacin and ceftriaxone was not followed by clinical improvement, and the child developed increased inflammatory indices (CRP 37 mg/dl, ERS 140 mm/h) and anemia (Hb 7.2 g/dl), which required a blood transfusion. Five days after admission, blood cultures yielded a methicillin-sensitive *S. aureus* (MSSA), resistant to ampicillin.

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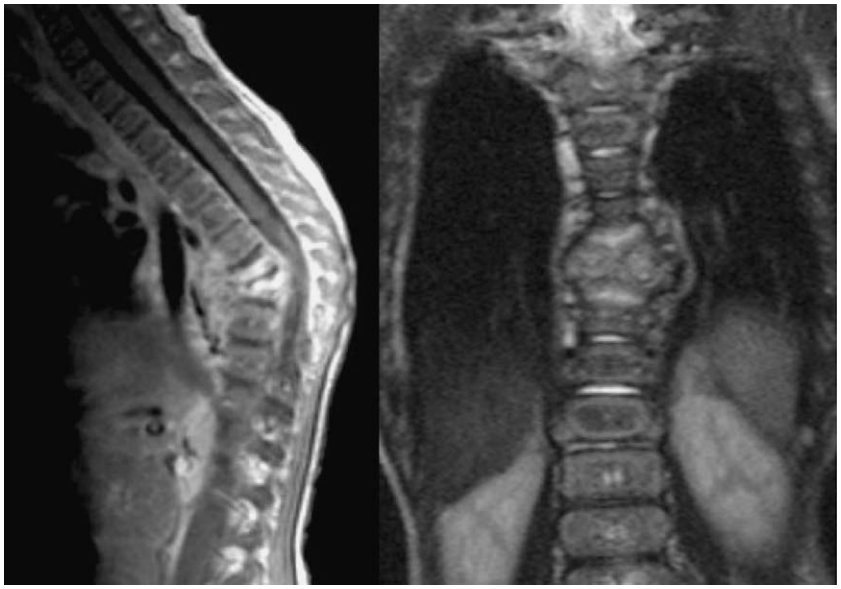

Figure 1. Thoracic (D8–D10) spondylodiscitis: magnetic resonance image at admission.

Susceptibility testing to vancomycin showed a minimum inhibitory concentration (MIC) of <2 μg/ml. Therefore, intravenous vancomycin was started (40 mg/kg divided into four daily doses). Following vancomycin treatment, the patient became afebrile and his leukocyte count (16.28×10^9/l, neutrophils 63%), ESR (85 mm/h) and CRP (15.5 mg/dl) decreased.

Nevertheless, the dorsal swelling increased in size, while ultrasound examination revealed a paravertebral inflammation. X-ray showed a reduced pulmonary infiltrate and a disk narrowing of the D8–D9 space. Computed tomography (CT) of the spine revealed rarefaction of the body of D9, with the infection spreading into the surrounding tissue. Bone scintigraphy, performed in order to detect multiple foci of infection, revealed increased signal intensity at the body and at the endplate of D9. Contrast-enhanced magnetic resonance imaging (MRI) showed destruction of D8, D9 and D10 with increased signal intensity in the sagittal T2-weighted image and tumefaction of surrounding tissue (Figure 1). Biopsy of the D8–D9 disc space was performed, but aerobic, anaerobic, fungal and mycobacterial culture failed to grow from the specimen. Histopathological examination revealed granulation tissue containing necrotic bone fragments and and inflammatory cells. After the exclusion of Langerhans cell histiocytosis and infantile myofibromatosis, an inflammatory process was confirmed.

About three weeks after starting vancomycin therapy, a sudden and progressive worsening of the clinical condition, with fever and a mild increment in the inflammatory indices (CRP 18 mg/dl, ESR 110 mm/h, white blood cell count 18.7×10^9/l with 75% polymorphonuclear neutrophils), was registered. A CT scan was performed and it showed no improvement in the lesions previously described. We suspected a therapeutic failure. A blood culture was performed and it showed no growth. We did not repeat a biopsy of the lesion. Taking into account the susceptibility to vancomycin of the previously isolated specimen, we thought that this failure could be ascribed to a low concentration of vancomycin in osteoarticular lesions. Considering both the susceptibility of the isolate to linezolid (MIC <0.5 μg/ml) and the high penetration of this molecule into the osteoarticular tissue, we decided to substitute vancomycin with linezolid, at a dosage of 30 mg/kg divided into three daily doses. This led to a reduction in the inflammatory indices and to a decrease of signal intensity in the sagittal T2-weighted image.

As a result of the improvement in clinical condition and in both the radiological and the laboratory findings, we decided to discontinue treatment after 27 days. Our choice not to continue the treatment was due to our limited experience with linezolid and to the risk of side effects in the case of a prolonged therapy. No diarrhea, hematological disorders, or other side effects were observed during the linezolid therapy.

Figure 2. Thoracic spondylodiscitis: magnetic resonance image after 2 years of follow-up.

In order to treat the kyphosis, a brace immobilization was carried out. Two years later, step-wise bony consolidation of the vertebral defect and partial remodeling was observed (Figure 2).

3. Discussion

Spondylodiscitis may be a complication of any systemic infection, but is frequently a primary solitary focus of disease. All types of microorganisms, including viruses, parasites, fungi, and bacteria, can cause spondylodiscitis.[3,7,8,12–15] *S. aureus* is responsible for 80–90% of cases of pyogenic osteomyelitis.[2,7,8] Its propensity to infect the bone may be related to the fact that it expresses receptors for bone matrix components such as collagen, thereby facilitating its adherence to bone tissue.[7,8,16,17] *S. aureus* can reach the bone by hematogenous spread, by extension from a contiguous site, and secondary to vascular insufficiency.[8] In our case, we could not find a primary source of infection, considering that there was neither evidence of skin superinfection nor history of trauma, central venous catheter, surgical or other invasive procedures. Although biopsy of the D8–D9 disc space was negative, blood cultures taken from a peripheral vein during an episode of fever became positive for *S. aureus*. In our patient, an MRI study of the spine appeared to be the best imaging study to evaluate possible vertebral osteomyelitis evolving from a discitis.[5,7,8,18] Blood cultures and more invasive procedures, including bone biopsy, should strongly be considered in patients with suspected vertebral osteomyelitis, where definition of a causal agent is particularly important for a correct selection of the appropriate antimicrobial therapy. Antibiotics were selected on the basis of the susceptibility testing. The first choice was vancomycin, which initially performed well: the patient underwent a consistent clinical improvement. However, after three weeks of therapy we observed a sudden worsening of the clinical condition of the patient, confirmed by imaging studies of the lesion. Possible explanations of this therapeutic failure could be a low concentration of vancomycin in osteoarticular lesions.

Linezolid is not approved for the therapy of osteoarticular infections, but on account of the high concentrations it can attain in osteoarticular tissue, and considering positive evidence from studies conducted in adult patients, it could be considered a good choice for pediatric bone and joint infections.[9] More studies are needed to confirm this observation. At the time of the clinical case described, our choice was probably not completely evidence-based, and an anti-staphylococcal penicillin or a first-generation cephalosporin would have been preferred.

Even if spondylodiscitis in the pediatric age-group is an extremely rare condition, it has to be considered in the differential diagnosis since an early diagnosis and an appropriate therapy are important to prevent potential complications, such as chronic infection, vascular necrosis, growth abnormalities, and neurological complications.[7,8,10,11]

Conflict of interest: No conflict of interest to declare.

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